Attorney Docket No. 04012.0188

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attached to Paper # 33

Applicant: Prieels _____, 1999

Serial No.: 08/909,879 Group Art Unit No.: 1648

Filed: August 12, 1997 Examiner: L. Smith

For: VACCINE COMPOSITION CONTAINING ADJUVANTS

Assistant Commissioner of Patents

Washington, D.C. 20231

DECLARATION OF DR. GERALD VOSS

1. I, Dr. Gerald Voss, a citizen of Germany and residing at , 12 Rue de la Barre, Grez-doiceau, Belgium, state and declare the following with respect to the invention described and claimed in U.S. Patent application No. 08/909,879 (Attorney Docket No. 04012.0188), entitled "VACCINE COMPOSITION CONTAINING ADJUVANTS."

2. I have received the following academic qualifications:

- Degree in Biology '83-'85, University of Freiburg, Germany.
- Master's degree in Biology (German diploma) '89, University of Goettingen, Germany
- Ph.D. in Biology '92, University of Goettingen and German Primate Centre, Goettingen.

I undertook a postdoctoral research position in Medicine, '93-'96, Harvard Medical School, Boston, USA. I joined SmithKline Beecham Biologicals in 1996, as a research group leader, specifically as an immunologist in the HIV, malaria, Dengue and adjuvant evaluation programs.

3. I filed a declaration in the subject application on May 22, 1998, in relation to my experience with HIV vaccines of the present invention, and showing therein the protection of Rhesus monkeys from experimental HIV infection by administration of vaccines of the present invention.

4. I have read and am familiar with the Office Action dated August 12, 1998, issued in the above captioned action. I understand that the Examiner has again rejected the claims, the objection being based at least in part on the examiners assertion that HIV specific CTL induced by the vaccine was not shown to reduce viral load or viral burden, or slow progression to AIDS.

5. In my opinion the subject patent and additional data described in my declarations clearly show that administration of the vaccines of the present invention are capable of (a) inducing protection from infection, or (b) reducing viral burden, and delaying detection of infection in those animals that are not fully protected.

6. I would like to note that the measurement of viral burden or viral load, is an assay which is commonly performed in investigative studies to measure any ameliorative effects of a therapeutic strategy which fails to provide protection. Accordingly, in animals which are protected from infection, there is no detectable viral burden or viral load. Likewise, in animal models which exhibit progression to AIDS-like symptoms, vaccinees that are protected, and therefore, do not show any viral load or viral burden, do not progress to AIDS in the absence of infection.

7. In the Rhesus monkey SHIV model described in my previous declaration, the vaccines comprising QS21 and 3D-MPL adjuvants have been shown to induce protection in two out of four vaccinees. Thus, in the two monkeys that were protected there was no detectable viral burden or viral load. This protection from infection was observed despite the lack of interpretable CTL data.

8. Also, the monkeys that were infected (2 out of 4) did in fact show a reduced viral burden as evidenced by delayed HIV Polymerase Chain Reaction (PCR) and reduced virus isolation (Quantative Virus Isolation (QVI)) in comparison to negative control animals. These results were published recently in Mooij *et al.*, 1998, AIDS, 12:F15-F22. A copy of this article is provided in Annex I.

9. In this paper, the group comprising gp120, 3D-MPL, and QS21 is group A. The results are summarised in Figure 1 (Cytokine assays, including IFNγ), Table 2 (humoral responses) and Table 3 (virus status post-challenge).

10. Also described in the same paper is a group wherein the adjuvant comprised QS21 and 3D-MPL in the form of an oil in water emulsion (Group B). This vaccine formulation resulted in the protection of all four animals of Group B from infection without any detectable viral load or viral burden (Table 3).

11. Furthermore, a third group of vaccinated animals (group C) is described in this article which were vaccinated with gp120 antigen together with QS21 and 3D-MPL in the form of an oil in water emulsion, this vaccine being given after a previous vaccination experiment with an unrelated weak adjuvant. This experiment demonstrated the ability of the adjuvant of the present invention to improve a previously existing weak anti-HIV immune response. All four of these animals were protected from viral challenge after the third administration of the QS21 and 3D-MPL containing vaccine.

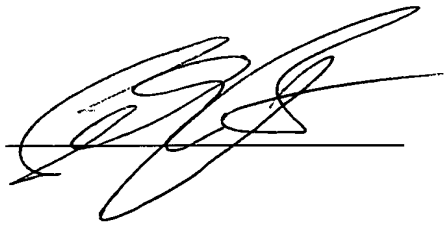
Conclusions

12. In conclusion, vaccines of the present invention, namely combinations of 3D-MPL and QS21, together with HIV antigen, have been shown to have efficacy in one of the best animal models currently available for the investigation of potential prophylactic HIV vaccines.

13. The Mooij *et al.* reference, therefore, describes twelve vaccinated animals which received a vaccine comprising HIV antigen, QS21 and 3D-MPL, 10 of which were protected from infection in the SHIV rhesus model. The remaining two animals showed reduced viral load and delayed onset of infection.

14. I declare that all statements made herein based on myown knowledge are

true and that all statements based on information and belief are believed to be true; and further that the statements are made with the knowledge that wilful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such wilful false statements may jeopardize the validity of the above application or any patent issued therefrom.



Date: January 15, 1999 Gerald Voss, Ph.D.